Evaluation for Perioperative Blood Transfusion during Major Abdominal Procedures in a Pediatric Population: A Retrospective Observation Cohort Study

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Keywords

Transfusion · Abdominal procedures · Overtransfusion · Inappropriate transfusion

Abstract

Objectives: The purpose of this study was to examine modifiable factors and their impact on perioperative blood transfusion for pediatric patients with major abdominal procedures. **Methods:** This is a retrospective review of 1,506 patients who underwent major abdominal surgical procedures in a tertiary medical center from January 2008 to June 2018. Clinical data about blood administration including triggers and targets for intra- or postoperative transfusion were collected and analyzed. The inappropriate transfusion (transfusion >8.0 g/dL of hemoglobin [Hb] trigger) and overtransfusion criteria (target transfusion >10.0 g/dL or >2 g/dL of target minus trigger level) were applied to examine the intraoperative factors with the intraoperative transfusion practice. Perioperative morbidity was further assessed based on the inappropriate transfusion and overtransfusion status. **Results:** Intraoperative transfusion was used in 468 (31.1%) of the 1,506 patients included in the study. Among them, 212 (45.3%) intraoperative transfusion episodes were classified as inappropriate, and 135 cases (28.8%) were confirmed as overtransfusion. On univariate analysis, inappropriate transfusions were observed more commonly among patients

with younger age ($p < 0.001$) and who underwent hepatic resection ($p < 0.001$) or intestinal resection ($p < 0.001$). Overtransfusion was also associated with elevated trigger of 8.0 g/dL Hb ($p = 0.006$) and younger age ($p = 0.003$). No perioperative complications were associated with inappropriate transfusions and overtransfusion under multivariate analysis. **Conclusions:** Overtransfusion was common in hepatic resection and younger age, but to definitely prove this hypothesis, a prospective randomized trial needs to be performed.

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Introduction

In the operating room, accounting for surgical blood loss and various clinical and laboratory values, transfusion of packed red blood cells (PRBCs) is often necessary to maintain hemodynamic stability and oxygen delivery. However, blood transfusion might be associated with febrile or allergic reactions, increased morbidity [1–3]. Due to the rapid nature of hemorrhage resuscitation, hemoglobin (Hb) triggers (the Hb level that prompts a PRBC

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transfusion) and intraoperative blood utilization vary significantly between different types of procedure because in some procedures, such as cardiac surgery, the bleeding can be rapid and may go undetected [4, 5]. In operations for gastrointestinal manipulation, the risk for perioperative hemorrhage is medium and should thus be stratified from other different types of surgery in terms of the transfusion algorithm.

To optimize blood transfusion, restrictive transfusion practices have been proposed and tested in various clinical scenarios, including intensive care, various surgeries, and situations with gastrointestinal bleeding [6–9]. Although the intraoperative Hb triggers and targets are less well defined, transfusion triggers of <7.0–8.0 g/dL and target levels between 7.0 and 9.0 g/dL have been found to be advantageous compared to liberal transfusion practice in stable condition and for the adult practice [10, 11]. We supposed that liberal transfusion in pediatric major abdominal procedures may be appropriate, but there was not enough evidence to support this aspect of transfusion practice in pediatric surgical practice.

Our study aimed to evaluate the role of intraoperative transfusion practices and to identify the ideal Hb range in postoperative recovery from general surgery. We assessed the variation of Hb triggers and overall utilization of intraoperative blood transfusion in pediatric patients undergoing gastroenterological surgery. We further evaluated perioperative outcomes in regards to inappropriate transfusion and overtransfusion.

Methods

Study Design

This is a retrospective observation cohort study.

Patient Selection

We performed retrospective transfusion analysis of documents regarding major abdominal operation at the Department of Pediatric General Surgery and Liver Transplantation, Children's Hospital, Chongqing Medical University from January 2008 to June 2018. Major abdominal surgery here were procedures involving the gastrointestinal tract that took >60 min. All patients who underwent elective Roux-en-Y hepaticojejunostomy, intestinal resection, or hepatic resection were considered eligible for entry into the study. The underlying diseases were biliary dilation for Roux-en-Y hepaticojejunostomy, strangulated intestinal obstruction, intestinal necrosis, or Meckel diverticulum for intestinal resection, and various benign or malignant hepatobiliary diseases for hepatic resection. All patients had to meet the following inclusion criteria: age 4 months to 6 years (within this age range, the normal Hb level is 100–160 g/L, which is different from other age groups) and normal preoperative renal function. Exclusion criteria included preexisting bleeding diathesis, PRBC transfusion before admission, severe sepsis, and steroid or immunosuppressive medication administration. The primary aim of this study was to examine the variables for intraoperative transfusion and overtransfusion for pediatric patients with major

abdominal procedures. The secondary aim was to determine the impact of intraoperative transfusion on postoperative morbidity.

Standard pre- and intraoperative variables were collected including demographic data, primary diagnosis and indication for surgery, clinical details and preexisting comorbidities, American Society of Anesthesiologists (ASA) classification, duration of operation, amount of intraoperative crystalloid and colloid fluid, estimated blood loss, intraoperative blood transfusion, intraoperative nadir Hb levels and Hb concentration at discharge, inpatient complications, and length of hospital stay. The number and volume of PRBC transfusions and other blood products (albumin, fresh frozen plasma, platelets, cryoprecipitate) were recorded.

In our institute, general anesthesia was usually performed using sevoflurane inhalation and intravenous propofol. Generally, the basis for intraoperative transfusion was the combination of a physiological transfusion trigger (generally Hb levels below or close to 8–9 g/dL) with a suspected or known comorbidity (hypotension, tachycardia, etc.). Specifically mentioned is that the smallest unit of PRBCs for transfusion is 50 mL (0.25 U) in our institute. No strict transfusion guidelines were followed in our institute. This means that blood transfusions were also performed as needed due to blood loss and to maintain hemodynamic stability without Hb level results. This principle was adhered to over the entire study period. In 2015, the intraoperative transfusion protocol was proposed based on the laboratory monitoring and hemodynamics parameters by the perioperative team. Hb concentration levels were to be obtained within 8 h before surgery or before each blood transfusion, immediately after each blood transfusion, and within 30 min postoperatively. PRBCs were generally transfused if the Hb level was <7–8 g/dL. The intraoperative Hb transfusion trigger was defined as the nadir intraoperative Hb level that preceded a blood transfusion. Following the blood transfusion, the intraoperative Hb level measured after transfusion was defined as the target Hb. For the purpose of the current analyses, an inappropriate Hb trigger cutoff value was defined as >8 g/dL, as established by previous data [1]. Overtransfusion was considered when the target Hb level was >2 g/dL above the relevant trigger level or a target Hb level >10.0 g/dL (Table 1).

Postoperative Complications

Complications only included grade II complications or higher, which are defined by the Clavien-Dindo classification system including major infections (sepsis, ventilator-associated pneumonia, and drug-resistant infections), gastrointestinal bleeding, abdominal abscess, venous thromboembolic disease, renal failure, and respiratory failure [12]. Major complications were defined as the following situations: need for repeat laparotomy, interventional radiology procedures, or requiring admission to the intensive care unit.

Statistical Analysis

Continuous variables were displayed as median (range) or as mean $\pm$ standard deviation. Variables were tested statistically with Mann-Whitney U test or Student *t* test, as appropriate. Categorical variables were described as frequencies (percentages) and were analyzed with χ^2 test or Fisher exact test, as appropriate. Multivariable risk-adjusted logistic regression models were further analyzed, with results reported as odds ratio (95% confidence interval). Factors included in the multivariable model were chosen from those that had a *p* value ≤ 0.1 in the bivariate analysis or were deemed clinically relevant. For all statistical analyses, a *p* value <0.05 was deemed significant. The SPSS 20.0 (IBM, Armonk, NY, USA) software was used to perform all statistical analyses.

Table 1. Clinical and operative characteristics based on perioperative PRBC transfusion

Perioperative red blood cell transfusion	Yes (<i>n</i> = 536)	No (<i>n</i> = 970)	<i>p</i> value
Age, years	4.85±2.69	4.88±3.57	0.28 ^a
Male:female ratio	305:231	569:401	0.27 ^b
Weight, kg	15.85±6.52	15.96±6.79	0.29 ^a
Intraoperative transfusion	468 (87.3%)	–	
Postoperative transfusion	68 (12.7%)	–	
Both intra- and postoperative transfusion	51 (9.5%)	–	
Operative time, min	126.79±58.24	114.85±49.26	0.26 ^a
Preoperative Hb level, g/dL	9.61±1.84	11.85±1.76	0.006 ^a
Estimated blood loss, mL	48.2±29.3	21.1±16.4	0.003 ^a
Operation type			
Roux-en-Y hepaticojejunostomy	293 (54.7%)	608 (62.7%)	0.079 ^b
Intestinal resection	151 (27.6%)	303 (31.2%)	0.001 ^b
Hepatic resection	92 (17.7%)	59 (6.1%)	<0.001 ^b
ASA classification			
ASA 1–2	127 (23.7%)	379 (39.1%)	<0.001 ^b
ASA 3–4	409 (76.3%)	591 (60.9%)	

Values are presented as mean ± standard deviation, *n/n*, or *n* (%). ASA, American Society of Anesthesiologists; PRBC, packed red blood cell. ^a Student *t* test. ^b χ^2 test or Fisher exact test.

Table 2. Clinicopathological and operative characteristics stratified by inappropriate (nadir Hb >8) or appropriate (nadir Hb <8) intraoperative transfusion

Characteristic	Appropriate (<i>n</i> = 256)	Inappropriate (<i>n</i> = 212)	<i>p</i> value
Age, years	3.8±1.2	1.3±0.6	<0.001 ^a
Male:female ratio	95:249	99:246	0.41 ^b
Preoperative Hb <12 g/dL	124	113	0.32 ^b
Operative time, min	122.1±57.6	129.2±58.2	0.18 ^a
Estimated blood loss, mL	46.8±23.5	52.6±22.1	0.13 ^a
Operation type			
Roux-en-Y hepaticojejunostomy	123 (48.0%)	102 (48.1%)	0.53 ^b
Intestinal resection	98 (38.3%)	53 (25.0%)	<0.001 ^b
Hepatic resection	35 (13.7%)	57 (26.9%)	<0.001 ^b
ASA classification ≥3–4	196 (76.6%)	159 (75.0%)	0.39 ^b

Values are presented as mean ± standard deviation, *n/n*, or *n* (%). ASA, American Society of Anesthesiologists; Hb, hemoglobin. ^a Student *t* test. ^b χ^2 test or Fisher exact test.

Results

Baseline Characteristics

A total of 1,506 patients were identified to meet the inclusion criteria between January 2008 and June 2018 in our institution. The most common operation was Roux-en-Y hepaticojejunostomy, followed by intestinal resection and hepatic resection. Among all patients, 536 (35.6%) received at least 0.25 unit of PRBC transfusion during their hospitalization. Conventional coagulation tests were used by >86% of the patients, whereas point of care monitoring systems were implemented only by 14% of the patients depending on specific monitoring condi-

tions. The median amount of PRBCs transfused was 0.5 unit (range 0.25–8 units), regardless of the timing of the transfusion (intraoperative vs. postoperative); specifically, 468 of 536 (87.3%) patients had intraoperative blood transfusion, 68 of 536 (12.7%) had postoperative blood transfusions, and 51 of 536 (9.5%) had both an intra- and postoperative blood transfusion. Several clinicopathological factors were associated with perioperative transfusion. Patients receiving a PRBC transfusion had lower preoperative Hb levels (9.61 ± 1.84 vs. 11.85 ± 1.76 g/dL, *p* = 0.006), higher operative blood loss (38.2 ± 23.3 vs. 21.1 ± 16.4 mL, *p* = 0.023), and a high ASA classification (*p* < 0.001) (Table 1).

Table 3. Outcome details based on inappropriate transfusion or overtransfusion

Characteristic	Inappropriate transfusion			Overtransfusion		
	yes (<i>n</i> = 256)	no (<i>n</i> = 212)	<i>p</i> value	yes (<i>n</i> = 135)	no (<i>n</i> = 333)	<i>p</i> value
Overall complications	100 (39.1%)	67 (31.6%)	0.057 ^b	57 (42.2%)	110 (33.0%)	0.039 ^b
Sepsis	36 (14.1%)	21 (9.9%)	0.11 ^b	22 (16.3%)	35 (10.5%)	0.060 ^b
Surgical site infection	41 (16.0%)	25 (11.8%)	0.12 ^b	28 (20.7%)	38 (11.4%)	0.008 ^b
Respiratory complications	22 (8.6%)	16 (7.5%)	0.41 ^b	13 (9.6%)	25 (7.5%)	0.28 ^b
Length of stay, days	12 (8–17)	11 (7–23)	0.10 ^a	13 (10–23)	11 (7–18)	0.093 ^a

Values are presented as *n* (%) or median (range). ^a Mann-Whitney U test. ^b χ^2 test or Fisher exact test.

Table 4. Univariable analysis of factors associated with overtransfusion

Characteristic	Overtransfusion		<i>p</i> value
	yes (<i>n</i> = 135)	no (<i>n</i> = 333)	
Age, years	2.9±1.1	2.2±0.9	0.003 ^a
Operative time, min	131.2±61.3	120.8±56.7	0.22 ^a
Preoperative Hb <12 g/dL	76 (56.3%)	161 (48.3%)	0.073 ^b
Estimated blood loss, mL	51.8±21.6	47.4±23.1	0.13 ^a
Trigger ≥8.0 g/dL	74 (54.8%)	138 (41.4%)	0.006 ^b
Operation type			
Roux-en-Y hepaticojejunostomy	60 (44.4%)	165 (49.5%)	0.18 ^b
Intestinal resection	52 (38.5%)	99 (29.7%)	0.042 ^b
Hepatic resection	23 (17.0%)	69 (20.7%)	0.22 ^b
ASA classification ≥3–4	108 (80.0%)	247 (74.2%)	0.11 ^b

Values are presented as mean ± standard deviation or *n* (%). ASA, American Society of Anesthesiologists; Hb, hemoglobin. ^a Student *t* test. ^b χ^2 test or Fisher exact test.

Based on Hb rationales, 212 of 468 (45.3%) intraoperative transfusion episodes were classified as inappropriate transfusions. Inappropriate transfusion stratified by various patient characteristics is shown in Table 2. On univariate analysis, inappropriate transfusions were observed more commonly among patients with younger age ($p < 0.001$) and who underwent hepatic resection ($p < 0.001$) or intestinal resection ($p < 0.001$).

Among the 468 patients who received an intraoperative transfusion, there was also a wide variation of transfusion target Hb levels, with a median of 9.7 g/dL (range 8.3–11.6 g/dL). Based on our criteria, 135 of 468 evaluable patients (28.8%) were overtransfused. Overtransfusion was more common among patients with an elevated transfusion trigger of 8.0 g/dL Hb ($p = 0.006$) and younger age ($p = 0.003$).

To investigate the factors that were associated with a higher risk of perioperative complications, we examined only the 468 patients with intraoperative transfusion. A total of 167 of 468 (35.7%) patients experienced at least one episode of grade II or higher complications. The most common complications were surgical site infection

(86/167, 51.5%), sepsis (57/167, 34.1%), and respiratory complications (38/167, 22.8%). We next stratified the cases into different complications. Patients with overtransfusion were associated with an increased rate of surgical site infection ($p = 0.008$) and overall complication pneumonia ($p = 0.039$) compared with those without overtransfusion (Table 3).

Multivariate analysis was conducted using a multivariable risk-adjusted logistic regression model that adjusted for the characteristics listed in Table 4. Iterative analyses of separate regression models for each of the individual complications listed in Table 3 revealed no significant associations with overtransfusion.

Discussion

This paper represents an initial attempt to analyze PRBC transfusion practice in a pediatric population during major abdominal surgery. By applying restricted Hb transfusion threshold and overtransfusion criteria, we also examined numerous demographic and perioperative

variables for possible associations with intraoperative PRBC transfusion among different types of major abdominal operation, which might help to optimize transfusion practice for the improvement of postoperative outcomes.

Despite several studies advocating for the restrictive use of PRBC transfusions [1, 11, 13], transfusion practice remains varied among different institutes, operations, and anesthesiologists [6, 14, 15]. Further expanding on this previous work, we showed significant variation in the transfusing trigger in the pediatric abdominal operation population even in our single department. Although we have changed the surgical and medical management from 2015, transfusion of red blood cells is usually required as before, with a high incidence of PRBC transfusion. Nearly one in seven individuals was transfused with an Hb trigger of ≥ 10 g/dL in the current cohort. Perhaps not surprisingly, the current patients with a lower preoperative Hb level and those with high estimated blood loss were significantly more likely to receive a blood transfusion. As most transfused patients in this study were anemic before surgery, it had been recommended that elective surgery be postponed to enable adequate patient preparation, which should avoid a certain extent of transfusion [16].

Although the current children had a relatively small blood volume, we considered that the current threshold of < 8 g/dL for transfusing red blood cells intraoperatively was appropriate and safe for the abdominal operation on stable condition, which was in accordance with recent recommendations [17, 18]. The postoperative complication incidence was identical between the two thresholds of < 8 g/dL and > 8 g/dL, which was consistent with other perioperative transfusion protocols based on lower transfusion criteria [11, 19]. According to the current results and our clinical experience, in the absence of active bleeding, transfusion is unnecessary with a recent Hb level > 8 g/dL. In most clinical trials, the common Hb transfusion triggers are 7.0 or 8.0 g/dL in the restrictive arms and 9.0 or 10.0 g/dL in the liberal arms [20, 21]. This low Hb threshold (7 or 8 g/dL) and a lower posttransfusion target of 10 g/dL (30% hematocrit) may not be acceptable for some specific type of surgery because the bleeding during the procedure can be rapid and may go undetected, like in cardiac surgery. We also believe that the risks outweighed the benefits to choose a lower trigger such as 6–7 g/dL even in the current pediatric cohort. The decision to transfuse blood intraoperatively is based on a multitude of factors, which includes not only the recently measured Hb, but also the elapsed time between the recently measured Hb, organ perfusion and hemodynamic stability, the current rate of surgical blood loss, which can sometimes be coupled with what point the surgeon is at in the procedure, as well as other surgical factors that may

modify the rate and amount of blood loss to be expected throughout the case (presence of abdominal adhesions, degree of observed coagulation, etc.).

There is growing evidence that overtransfusion of PRBCs might cause harm [18, 22–24]. Although overtransfusion was difficult to define in the pediatric population, we still adopted the common definition used in the adult reference to identify various factors related to potential overtransfusion in the operating room in a pediatric population. The 2 g/dL target zone was previously considered to underestimate the actual level of overtransfusion. Another criterion for overtransfusion was a posttransfusion Hb target of 10 g/dL (30% hematocrit) [24], which was adopted in the current research as to delineate overtransfusion. The current levels of overtransfusion should be practicable because the complication incidences were also identical based on whether there was overtransfusion or not. This traditional target of 10 g/dL may be perpetuating overtransfusion, particularly among patients with a low Hb threshold (7 or 8 g/dL) where a lower posttransfusion target may be acceptable. A previous report found that 19% of patients undergoing elective surgery were overtransfused [25], which is similar to what was observed in the current study (28.8% of patients were determined to be overtransfused according to the current criterion).

We found that although much variation existed with intraoperative blood utilization, the key risk factors for overtransfusion in a multivariable regression model included an elevated transfusion trigger, younger age, and a hepatic resection procedure. As mentioned previously [23], those of lower weight were at highest risk of overtransfusion. As female patients are typically lighter than males, the lighter females are more likely to exceed the target Hb than the heavier males with the same pretransfusion Hb level when a similar volume of blood is transfused. We really did not find an association between female sex and overtransfusion, but we did find that younger age was a factor related with overtransfusion, in the same way as what has been seen in adults.

Since this patient population typically weighs approximately 5–15 kg, a 10 mL/kg bolus of PRBCs in some cases may exceed the volume of the smallest unit, which is 50 mL (0.25 U). When for the case the Hb or blood pressure is borderline, most anesthesiologists prefer to transfuse the rest of current blood to prevent wastage if there are no signs of volume overload, otherwise the remaining red cells must be discarded since their shelf life is only 4 h after the initiation of the transfusion. This decision may result in qualifying as an overtransfusion according to the current criterion, which may be a benefit and prevent further donor exposure from a new unit of blood in the postoperative period when an expected amount of postoperative bleeding has occurred. We acknowledge that in clinical

practice, it should not be considered inappropriate in some cases, which should be analyzed under the specific situation.

Previous research suggested the association of intraoperative transfusion and increased perioperative morbidity and mortality [26, 27]. The present data provide further insight into the association of inappropriate transfusion and overtransfusion with perioperative complications. These complications were driven largely by infectious complications such as nosocomial infections, viral infections, sepsis, transfusion-related acute lung injury, etc. Although our study was not powered to show an unfavorable effect of overtransfusion in terms of perioperative morbidity, decreasing blood transfusion may at least have benefit for saving blood, which was associated with mean costs per patient.

The present study has certain limitations that need to be considered when interpreting the data. First, the data were collected retrospectively from a single institution with various shifting patients; although we did perform a power analysis, this was still a relatively small single-center study. In practice, there is no executable guideline for transfusion therapy in pediatric patients. The decisions for transfusion were not solely based on laboratory findings, but on case-specific factors such as anticipated future blood loss as well as the physician's experience and personality. Furthermore, some hemodynamic parameters were not evaluated here, which could have been important in determining the amount of PRBCs administered. Hence, caution should be used when interpreting our findings.

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Conclusion

The variation in transfusion practice might originate from transfusion trigger, operation type, body size, and even the anesthesiologist's preference due to the lack of common guidance. A transfusion algorithm of appropriate Hb range and trigger to save transfusion without compromising clinical outcomes should be developed and assessed in further research in the pediatric population.

Statement of Ethics

The institutional review board of Children's Hospital, Chongqing Children's Hospital gave expedited approval to review the medical records of surgical patients who had undergone major abdominal surgery. The patients were not required to provide written informed consent for this study.

Disclosure Statement

No potential conflicts of interest relevant to this article are reported.

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